and no dispersion, which is indicative of a collapsed but disordered and fluctuating structure or non-specific association. All seven mutant proteins retain their ability to bind IgG as measured by binding to an IgG-Sepharose affinity column. The stability and native-like character of $\Delta h_{0.9}$[-1.50Å] and $\Delta h_{1.0}$[+1.50Å] indicate that the sequence selection algorithm is sufficiently robust to tolerate Δh perturbations that are as large as 15% of Gβ1's native height super-secondary structure parameter value of 10 Å.--

A8 cancel

In the Claims:

Please cancel claim 1 without prejudice or disclaimer.

Please add the following claims:

A9

--30. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure;

(C) establishing a group of potential amino acids for each of said variable residue positions; and

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes a Dead-End Elimination (DEE) computation.

SUB B1

31. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

AG cntd

(A) receiving a protein backbone structure with variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure prior to establishing a group of potential amino acids;

(C) classifying each variable residue position as either a core, surface or boundary residue;

SUB B' CD J.t.

(D) establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has an amino acid selected from each of at least two different amino acids; and

(E) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein to generate a set of optimized protein sequences.

32. A method according to claim 31 wherein said analyzing step comprises a DEE computation.

33. A method according to claim 30 or 32 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

34. A method according to claim 30 or 32 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

A9. cont'd

35. A method according to claim 30 or 32 wherein said analyzing step includes the use of at least one scoring function.

SUB B' cont.

36. A method according to claim 35 wherein said scoring function is selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

37. A method according to claim 35 wherein said analyzing step includes the use of at least two scoring functions.

38. A method according to claim 35 wherein said analyzing step includes the use of at least three scoring functions.

39. A method according to claim 35 wherein said analyzing step includes the use of at least four scoring functions.

40. A method according to claim 35 wherein said atomic solvation scoring function includes a scaling factor that compensates for over-counting.

SUB B2

41. A method according to claim 30 or 31 further comprising experimentally testing at least one member of said set.

42. A method according to claim 33 further comprising the step of:

A9 cont'd

generating a rank ordered list of additional optimal sequences from said globally optimal protein sequence.

43. A method according to claim 42 wherein said generating includes the use of a Monte Carlo search.

44. A method according to claim 31 wherein said analyzing step comprises a Monte Carlo computation.

SUB B3

45. A method according to claim 42 further comprising the step of:

testing some or all of said protein sequences from said ordered list to produce potential energy test results.

46. A method according to claim 45 further comprising the step of:

analyzing the correspondence between said potential energy test results and theoretical potential energy data.

SUB B4

47. A recombinant protein comprising an optimized protein sequence generated by the method of claim 30 or 31.

48. A nucleic acid sequence encoding a recombinant protein according to claim 47.

49. An expression vector comprising the nucleic acid sequence of claim 48.

A9 cont'd

50. A host cell comprising the nucleic acid sequence of claim 48.

51. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) altering at least one supersecondary structure parameter value of said protein backbone structure;

(C) establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has a amino acid selected from each of at least two different amino acids; and

(D) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes:

i. a Dead-End Elimination (DEE) computation; and,

ii. at least one scoring function selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

52. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

A9 contd

(B) altering at least one supersecondary structure parameter value of said protein backbone structure;

(C) classifying each variable residue position as either a core, surface or boundary residue;

(D)establishing a group of potential amino acids for each of said variable residue positions, wherein the group of potential amino acids for at least one of said variable residue position has a amino acid selected from each of at least two different amino acids; and

(E) analyzing the interaction of all or part of each of said amino acids with all or part of the remainder of said protein to generate a set of optimized protein sequences wherein said analyzing step includes:

i. a Dead-End Elimination (DEE) computation; and,

ii. at least one scoring function selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.--

A9 cancel